Remarks

Claim 8 has been amended and presented as new claim 20. The amendments to claim 8 are the addition of a 95% homology standard (up from 85% in the original claim; basis specification page 3 line 10), addition of a hOAT functionality recitations (basis specification page 5 lines 4-11), and exclusion of related prior art sequences (basis specification page 3 lines 14-18).

Claim 21 is substantively identical to original claim 9.

Claims 15-16 and 19 were withdrawn from consideration as non-elected inventions. These claims have been cancelled in this amendment.

The Examiner should be aware that "isolated" polypeptide is hOAT which is separated from its normal cellular environment as it is found in nature (specification page 4, lines 3-5). This does not mean that the polypeptide must be isolated in the chemical sense, only that the claimed polypeptide is not present in its normal human kidney cell environment. The recitation "isolated" is used solely to provide novelty over hOAT in situ as a natural product, i.e., normal human kidney cells.

Claim 8 was rejected under 35 USC 112(1) as nonenabling for variants of hOAT. The Examiner urges that even minor sequence changes can exert profound effects on protein function, and that Applicants have offered insufficient guidance for introducing sequence variants (due to the absence of a detailed structure/function analysis of the protein). The Examiner particularly notes that the claims contain no functional limitation for the variants and fail to state what distinguishing attributes are shared by the genus of variants. The Examiner opines that the specification fails to teach how to

make and use the variants (although the Examiner does concede that it teaches how to screen for activity). Finally, the Examiner observes that the claims do not limit the number of changes and do not describe the common attributes or characteristics that identify the members of the hOAT genus of variants.

Claim 8 has been amended in such a fashion as to address all of these concerns. The primary issue, which appears to concern the Office, is the absence of any recited characteristic for the hOAT polypeptide. This has been remedied by reciting two properties for any claimed hOAT polypeptide, at least one of which will be possessed by each variant falling within the scope of the claims. These are organic ion transport and/or immune cross-reactivity with the native/reference sequence of SEQ ID NO. 2.

The specification in Example 1 discloses how to produce recombinant hOAT by expression in host cells. Note that hOAT expressed within CHO cells (but not recovered per se from those cells) meets the limitations of claim 8. Thus, the specification discloses how to make hOAT and its 95% homologous variants.

Insofar as using hOAT and its variants, the Examiner's attention is directed to the process of Example 2. This illustrates how to test the hOAT for its ability to transport organic ions. Example 3 shows how to use an antibody directed against native hOAT in analysis of immunocross-reactivity of the recombinant hOAT.

The Examiner notes that the specification offers insufficient structural information to make variants having desired characteristics. There might be some merit to this point if a polypeptide was solely and exclusively defined in terms of enzyme activity or other structurally sensitive feature. However, claim 8 has been amended to

recite that the variants, in effect, possess a shared immune epitope with native hOAT. This is quite a modest hurdle since immune epitopes are generally known to contain as few as 5 to 10 residues, and claim 8 does not call for identical immunoaffinity between the native and variant sequences. No doubt, some scattered sites will be critical for either ion transport. However, it would be quite a challenge to make a polypeptide that would fail to possess even one immune epitope in common with native hOAT.

Enablement does not require absolute predictability of outcome. All that is necessary is that the Applicant supply the tools to obtain polypeptides meeting the claim recitations without undue experimentation, and the specification does this. It is axiomatic that the experimentation may be quite extensive so long as it is routine. Nothing could be more routine than making, expressing and testing the variants of this invention. While some may not even meet the modest standards of the claims, Applicant would be hard pressed to believe that any significant number would either fail to transport anions or be cross-reactive.

The rejection for lack of enablement is now believed to be moot.

Claim 8 was rejected under 35 USC 112(1) as failing to provide a written description of the claimed genus. This rejection is traversed on the same grounds noted above. The Examiner points out that this rejection can be overcome by disclosure of relevant identifying characteristics, including functional characteristics coupled with known or disclosed correlation between structure and functional structure or by a combination of such characteristics. Claim 8 now recites functional characteristics, and the specification teaches that hOAT is a multiple transmembrane spanning polypeptide,

a structural feature. Information that the protein contains multiple membrane spanning sequences (easily identified by their relative hydrophobicity) is useful in selecting sites of variation that will not be solvent exposed and thus be immunologically masked. Such variants then would be more likely to possess residual immunorecognition sites. Again, a specification is not a cook book. It presumes that one skilled in the art would apply conventional abilities to selecting suitable sites of variation. It is not necessary that the written description of the invention be so detailed as to exclude any independent exercise of skill by the artisan. It only need provide a reasonable level of guidance. This rejection is now believed to be moot in light of the amendments to the claims.

Claim 8 was rejected under 35 USC 112(2) as vague and indefinite for the term "hOAT," the Examiner pointing out that this term has been used for a chemical compound. This rejection is now believed to be moot since Claim 8 now clearly recites that the claimed substance is a polypeptide having a high degree of homology with that of SEQ ID NO 2. No one could be possibly confused any longer that the claimed subject matter is a low molecular weight compound.

Claim 8 was rejected under 35 USC 102 as anticipated by rat OAT of Sekine et al. Claim 8 now expressly excludes this protein, both because it does so expressly and because the degree of homology is now 95%, well beyond the 89.5% homology of rat OAT to hOAT of SEQ ID NO 2. This rejection is now believed to be moot.

This application is now believed to be in condition for allowance. An early Notice to that effect is solicited.

Respectfully submitted,

Mark L. Bosse
Reg. No. 35,071
Phone: (650) 522-5569
Fax: (650) 522-5575
email: mark.bosse@gilead.com
Date: May 14, 2004